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APPENDIX. CONFERENCE DISCUSSION

Dr N. Bonaros (Innsbruck, Austria): This is a solidly designed study with good statistical methods and good results. I have a comment and a question.

Five out of six observational studies included in this report were performed in an era before the introduction of the SYNTAX score as an assessment parameter of the complexity of coronary lesions; thus, in 1588 out of 2885 patients, the decision for stratification to MIDCAB or PCI was mainly based on the feasibility of performing PCI or not. This leads us to the suspicion that easy PCI targets, which we would now call low SYNTAX score targets, were treated with PCI and thus were included in the PCI group, while difficult PCI targets, now called high SYNTAX score lesions, were treated by surgical revascularization. With this in mind, do you think that this meta-analysis should include both prospective randomized and observational data?

And my comment: in your abstract conclusions you state that this meta-analysis underscores the superiority of MIDCAB over PCI for the treatment of single-vessel disease. Similar to the one-year results of the SYNTAX trial, surgical revascularization has proven to be superior in terms of MACCE. Do you still think that?

Dr Deppe: Regarding your question, it is correct that most of the studies in our meta-analysis were published before the SYNTAX score was established and therefore this tool was not available. I'm not sure if I completely understood your comment, but I still believe in the superiority of the mammary artery compared with PCI and stenting and our data suggest that you should revascularize the left anterior descending artery with a graft surgically.

Dr S. Head (Rotterdam, Netherlands): If I may comment on the last question. The SYNTAX score actually is applicable to patients with 3-vessel disease or left main disease. So in patients with isolated LAD it may not be the most appropriate score to guide the decision-making between patients that undergo PCI or CABG. Of course, as you said, there may be some differences

in observational studies as to which patients underwent PCI and which patients underwent CABG. But the SYNTAX score doesn't translate to these patients. It's only validated in patients with 3-vessel or left main disease, and therefore we're not so sure whether it would actually work in isolated LAD as well.

Dr Bonaros: I think the SYNTAX score is, of course, a good tool. The thing is that the decision-making back then in the observational studies was based on the complexity of the lesion. So I don't think that an invasive cardiologist back then would make the decision to perform a highly complex PCI intervention in a patient, but would rather send the patient for a MIDCAB. So this is the reason I think we have to probably improve the validation of the results by excluding the observational studies from the meta-analysis.

Dr D. Taggart (Oxford, UK): I believe the mean follow-up for these patients was two years; is that correct?

Dr Deppe: Yes, that's right. There was one study reporting the 10-year results, but most of the studies stopped follow-up after 12 or 24 months.

Dr Taggart: I think this is very important in the interpretation of this data. If we look at SYNTAX at five years for 3-vessel disease, there is a significant survival advantage in patients with SYNTAX scores above 22. But if you look at those same patients at 1, 2 or 3 years, there is no difference in survival. And it's only with further duration of follow-up that you begin to also see survival advantage of CABG.

So, for example, there are now 13 propensity-matched registries in the literature containing 433,000 patients comparing CABG and PCI, and every one of them shows a survival advantage from 5 to 7 percentage points at 5 years. But if you look at those registry rates at 1, 2 or 3 years, there is no difference in survival. And we have to get away from the mentality of now making CABG an intervention that we define with one- or two-year outcomes. That's particularly so now when you look at the evidence in the literature showing patency of mammary arteries to the LAD of over 90% at 20 years of follow-up.

So we have to be very careful how we present this. Because this type of data will be used by cardiologists to quote this paper and say, 'Look, no difference between CABG and PCI.' And it's long-term follow-up for the cardiologists because it's two years, so we have to be careful.

As we finish, I would like to ask the audience 'Who believes that all patients with proximal LAD disease should at least be discussed in terms of having a mammary artery rather than just being stented?' (Show of hands.) Oh, more convincing. Then, let me ask you, 'Who believes that patients with complex disease of the proximal LAD should always be offered the benefit of a discussion about a mammary artery?' (Show of hands.) Good. Thank you very much for your presentation.

Surgical or percutaneous revascularization for isolated left anterior descending stenoses: are we in the same boat?

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Ischaemic lesions located in the proximal left anterior descending (LAD) coronary artery are present in approximately 10% of patients with stable coronary artery disease requiring myocardial

revascularization. In view of the associated prognostic benefit, the current joint guidelines of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery

(EACTS) recommend myocardial revascularization with a Class I and a level of evidence A for patients presenting with an isolated >50% stenosis of the proximal LAD [1]. The optimal revascularization strategy for these lesions, however, is still a matter of debate. Surgical revascularization with minimally invasive direct coronary artery bypass grafting (MIDCAB)—through a small left anterior thoracotomy—has been developed to minimize surgical procedure invasiveness and has effectively reduced the procedural complications associated with conventional coronary artery bypass surgery (CABG) [2]. Alternatively, contemporary percutaneous coronary interventions (PCIs) allow for a prompt revascularization procedure with a catheter-based dilatation of the coronary stenosis optimized by the implantation of a drug-eluting stent (DES) [3].

In this issue of the *European Journal of Cardio-Thoracic Surgery*, Deppe *et al.* report the findings of a meta-analysis of 12 studies—including a total of 2885 patients—directly comparing MIDCAB with PCI for the treatment of isolated proximal LAD disease [4]. The authors observed no significant differences between the two revascularization modalities with respect to mortality [odds ratio (OR) 0.98, 95% confidence interval (CI) 0.70–1.39], cardiac mortality (OR 0.95, 95% CI 0.52–1.76), myocardial infarction (OR 1.05, 95% CI 0.71–1.56) and stroke (OR 1.22, 95% CI 0.60–2.48) during long-term follow-up. However, PCI resulted to be associated with a shorter length of hospital stay (weighted mean difference –3.37 days, 95% CI –4.92 to –1.81 days) and a higher risk of target-vessel revascularization (OR 3.80, 95% CI 2.82–5.10) when compared with MIDCAB.

The findings of this meta-analysis need to be interpreted in light of two important considerations. Firstly, Deppe *et al.* included both randomized, controlled trials and observational studies in their meta-analysis. This approach is methodologically debatable as it may determine very precise but equally spurious results due to confounders and selection bias [5]. Secondly, the authors included any PCI strategy in the meta-analysis—ranging from plain balloon angioplasty to DES implantation—despite significant changes in treatment effects have been consistently shown with PCI technological evolution [3]. Contemporary PCI is based on the implantation of DESs, which have significantly improved safety and efficacy outcomes compared with bare metal stents or plain balloon angioplasty [6, 7]. Therefore, pooling these different percutaneous revascularization modalities in one single treatment group does not adequately reflect contemporary clinical practice, impairing the interpretability of the meta-analysis findings. As a matter of fact, the significant heterogeneity observed by the authors for almost all the analysed outcomes is—at least in part—a result of these two key limitations. It should also be emphasized that adequate training and experience are key factors to achieve high procedural success of MIDCAB, with patency rates of the LAD anastomoses as high as those achieved with conventional CABG.

Keeping in mind these considerations, the findings of Deppe *et al.* provide important information. The absence of any differences in the risks of mortality, myocardial infarction and stroke between PCI and MIDCAB during long-term follow-up is a relevant piece of evidence, which highlights that excellent minimally invasive treatment options are available for patients with isolated proximal LAD disease. As it relates to the risk of target-vessel revascularization, the results are obviously biased by the mixture of PCI modalities. The use of contemporary DESs has consistently reduced the occurrence of restenosis and subsequent need for

repeat revascularization by over 80% when compared with bare metal stents [8, 9]. In view of this well-established benefit of DESs, the authors' findings with respect to target-vessel revascularization should be interpreted with particular caution. As shown by the authors in a sensitivity analysis, the risk of target-vessel revascularization did not significantly differ between PCI with DES compared with MIDCAB (OR 3.50, 95% CI 0.98–12.52). Certainly, this sensitivity analysis suffers from an imprecise point estimate with a wide confidence interval. In addition, the limited number and size of randomized trials directly comparing DESs and MIDCAB does not allow definitive conclusions. However, the available comparative evidence is reassuring on the similar safety and efficacy profile of PCI with DES and MIDCAB in patients with isolated proximal LAD disease. This is reflected by the most recent joint guidelines on myocardial revascularization of the ESC and EACTS that provide the same class of recommendation (I) and level of evidence (A) for both PCI with DESs and coronary artery bypass surgery for the treatment of patients with isolated proximal LAD disease [1].

In summary, the findings of Deppe *et al.* show that surgical and percutaneous minimally invasive treatment strategies can be offered with excellent long-term clinical outcomes. Given that myocardial revascularization is recommended in patients with isolated proximal LAD lesions, the optimal treatment choice should be based on patients' preference, clinical and anatomical characteristics, hospital and physician expertise and local Heart Team protocols. Cardiovascular surgeons and interventional cardiologists should work in liaison in order to offer the best available minimally invasive treatment strategies since 'no matter by what various crafts we came here, but are all now in the same boat' [10].

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